PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference P962-PCT	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/006229	24.03.2005	24.03.2004

International Patent Classification (IPC) or both national classification and IPC

Applicant
CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/006229

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
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International application No.
PCT/JP2005/006229

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-6	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-6	NO
Industrial applicability (IA)	Claims	1-6	YES
	Claims		NO

2. Citations and explanations:

Document 1: JP 05-227970 A (Chugai Pharmaceutical Co., Ltd.) 07 September 1993, paragraphs 0140-0143, 0170-0171 & WO 1992/019759 A1, line 3 on page 64 to line 15 on page 65, example 10 & US 5795965 A1 & EP 0628639 A1

Document 2: JP 2002-510211 A (Genentech Incorporated) 02 April 2002, line 14 on page 77 to line 10 on page 79, & WO 1999/001556 A2 & US 5994511 A1

Document 3: MERKLER, et al., Recombinant type A rat 75-kDa alpha-amidating enzyme catalyzes the conversion of glycine-extended peptides to peptide amides via an alpha-hydroxyglycine intermediate, Arch. Biochem. Biophys., Vol. 289, No. 1, 15 August 1991, p. 192-196

Document 4: MILLER, et al.; Characterization of a bifunctional peptidylglycine alpha-amidating enzyme expressed in Chinese hamster ovary cells, Arch. Biochem. Biophys., Vol. 298, No.2, 01 November 1992, pp.380-388

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Document 6: JP 2002-525104 A (SmithKline Beecham Corporation) 13 August 2002, paragraph 0123 & WO 2000/018804 A1 & US 6365154 B1

Document 7: JP 06-319396 A (Japan Tobacco, Inc.) 22 November 1994, paragraph 0028 (Family: none)

Document 8: ADAMCZYK, et al., Complete sequencing of anti-vancomycin fab fragment by liquid chromatography-electrospray ion trap mass spectrometry with a combination of database searching and manual interpretation of the MS/MS spectra, J. Immunol. Methods, Vol. 260, No. 1-2, 01 February 2002, pp. 235-249

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Claims 1-6

The inventions described in claims 1-6 do not appear to involve an inventive step based on documents 1-8 cited in the ISR.

Document 1 describes a method for producing a humanized PM-1 antibody using CHO cells (see paragraphs 0140-0143 and 0170-0171). In addition, document 2 indicates amidation of the C terminus of a carboxyl group as chemical modification of an antibody, and documents 3-5 describe methods of amidating the C terminus of a peptide amidated on the peptide C terminus wherein peptidylglycine α-amidating enzyme is used to cleave glycine present at the C terminus as a method of performing amidation of a C terminus carboxyl group.

Here, subclasses 1 and 2 of humanized PM-1 antibody in the invention of the present application are matters wherein the heavy chain C terminus of the constant region not needed for antigen recognition is amidized. The possibility of preserving the activity of an antibody prior to modification even if chemical modification of the constant region not needed for antigen recognition is performed is common general technical knowledge in the relevant field, and thus amidation of a heavy chain C terminus of said antibody using a method described in documents 3-5 in order to make a humanized PM-1 antibody by a method described in document 1 and modify a heavy chain C terminus that is not needed for antigen recognition would be easy for an expert in the relevant technical field.

In addition, because it well known that an antibody heavy chain N terminus may be pyroglutamate (see documents 6-8, for example), acquisition of a pyroglutamate antibody by a heavy chain N terminal would be easy for an expert in the relevant technical field. Furthermore, making a pharmaceutical composition comprising humanized PM-1 antibody subgroups would also be easy for an expert in the relevant technical field.

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